IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

EXELIXIS, INC., Plaintiff, v. MSN LABORATORIES PRIVATE LIMITED and MSN PHARMACEUTICALS, INC., Defendants.	)	C.A. No. 22-228 (RGA) (JLH) **CONSOLIDATED**

EXELIXIS' OPENING POST-TRIAL BRIEF
ON INFRINGEMENT OF U.S. PATENT NO. 11,298,349

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

TABLE OF ABBREVIATIONS

Abbreviation	Description
’439 patent	U.S. Patent No. 11,091,439 (JTX-001)
’440 patent	U.S. Patent No. 11,091,440 (JTX-002)
’015 patent	U.S. Patent No. 11,098,015 (JTX-003)
’349 patent	U.S. Patent No. 11,298,349 (JTX-004)
1-1 impurity	6,7-dimethoxy-quinoline-4-ol
ANDA	Abbreviated New Drug Application
API	Active Pharmaceutical Ingredient
Asserted Claims	For the ’349 patent, claim 3 For the ’439 patent, claim 4 For the ’440 patent, claim 3 For the ’015 patent, claim 2
Exelixis	Exelixis, Inc.
FDA	United States Food and Drug Administration
FOF	Exelixis’ Proposed Findings of Fact on MSN’s Infringement
GRASTAR	Granulated corn starch
MSN	MSN Laboratories Private Limited and MSN Pharmaceuticals, Inc.
MSN’s ANDA	MSN ANDA No. 213878
NDA	New Drug Application
POSA	Person of ordinary skill in the art
Tr.	Final Trial Transcripts
UF	Uncontested Facts (D.I. 154, Ex. 1)
Zydus	Zydus Worldwide DMCC

I. INTRODUCTION

In this Hatch Waxman case, Plaintiff Exelixis, Inc. ("Exelixis") asserts that MSN Laboratories Private Limited and MSN Pharmaceuticals, Inc. (collectively, "MSN") infringe claim 3 of U.S. Patent No. 11,298,349 ("the '349 patent"). The '349 patent is directed to a pharmaceutical composition of cabozantinib (L)-malate that includes certain classes of excipients and is free of a harmful genotoxic impurity. To determine infringement, the Court must decide one issue: whether the granulated corn starch (GRASTAR) in MSN's proposed generic products is a glidant. The evidence—including MSN's statements to the Food and Drug Administration (FDA)—proves that the GRASTAR in MSN's generic products is a glidant and that MSN infringes the '349 patent.

II. NATURE & STAGE OF THE PROCEEDINGS

Exelixis develops therapies for hard-to-treat cancers. UF ¶ 2; FOF ¶ 1. After discovering the new chemical entity cabozantinib in 2003, Exelixis scientists spent years developing pharmaceutical compositions of cabozantinib that would be safe and effective for patients. FOF ¶ 2. The company's resulting Cometriq® capsules and Cabometyx® tablets, both of which contain cabozantinib, were approved by the FDA in 2012 and 2016, respectively. UF ¶¶ 48, 58; FOF ¶ 3. Since then, Cabometyx® has become the preferred treatment for certain kidney, liver, and thyroid cancers and has been used to treat over 55,000 patients in the United States alone. FOF ¶ 3.

In 2019, MSN submitted Abbreviated New Drug Application (ANDA) No. 213878 seeking to market generic versions of Cabometyx® ("ANDA Products"). UF ¶ 6; FOF ¶ 6. In a prior action, the Court held that MSN's ANDA Products infringe Exelixis' U.S. Patent No. 7,579,473, which covers cabozantinib. D.I. 331 (Final Judgment), *Exelixis, Inc. v. MSN Lab'ys Private Ltd. & MSN Pharms., Inc.*, C.A. No. 19-2017 (Jan. 30, 2023).

In the instant suit filed in 2022, Exelixis asserts that MSN infringes claim 3 of the '349 patent, which is directed to a formulation of cabozantinib free of a specific genotoxic impurity. UF ¶ 41; FOF ¶ 13. MSN disputes infringement and asserts that claim 3 of the '349 patent is obvious in view of the prior art. Exelixis also asserts infringement of three patents directed to crystalline cabozantinib (L)-malate and uses thereof, including claim 4 of U.S. Patent No. 11,091,439 ("the '439 patent"), claim 3 of U.S. Patent No. 11,091,440 ("the '440 patent"), and claim 2 of U.S. Patent No. 11,098,015 ("the '015 patent") (the '439, '440 and '015 patents are collectively referenced as "the Crystalline Malate Salt Patents"). UF ¶¶ 20, 22, 24; FOF ¶ 4; D.I. 1 (Complaint), *Exelixis, Inc. v. MSN Lab'ys Private Ltd. & MSN Pharms., Inc.*, C.A. No. 22-cv-228-RGA (Feb. 23, 2022); D.I. 1 (Complaint), *Exelixis, Inc. v. MSN Lab'ys Private Ltd. & MSN Pharms.*, Inc., C.A. No. 22-cv-945-RGA (July 18, 2022). MSN has stipulated to infringement of the Crystalline Malate Salt Patents but challenges the validity of the asserted claims.

The Court held a bench trial from October 23 to 26, 2023. This opening post-trial brief addresses infringement of claim 3 of the '349 patent—the only issue on which Exelixis bears the burden of proof, given MSN's stipulation of infringement of the Crystalline Malate Salt Patents. The brief is accompanied by Exelixis' proposed Findings of Fact ("FOF") relating to infringement.

III. SUMMARY OF ARGUMENT

Claim 3 of the '349 patent recites a tablet pharmaceutical composition of cabozantinib (L)-malate that includes a filler, lubricant, disintegrant, and glidant and is essentially free of 6,7-dimethoxy-quinoline-4-ol (the "1-1 impurity"), a genotoxic impurity. MSN has stipulated that its ANDA Products are cabozantinib (L)-malate tablets containing a filler, lubricant and disintegrant, and are essentially free of the 1-1 impurity. The only disputed infringement issue is whether MSN's ANDA Products include a "glidant." As set forth below, the evidence at trial clearly established that the GRASTAR in MSN's ANDA Products is a glidant.

First, there is no dispute that a glidant is a substance that improves the flow characteristics of a powder mixture. Both parties' formulation experts and MSN's Head of Formulation Research and Development endorsed this well-established, plain and ordinary definition.

Second, as MSN repeatedly told the FDA in its ANDA submission, the GRASTAR in its ANDA Products plays an important role in improving the flow characteristics of MSN's formulation. This is not surprising given that the active pharmaceutical ingredient (API) cabozantinib (L)-malate flows poorly, a property that can be addressed by including a glidant in the formulation. And starch and starch derivatives like GRASTAR are known glidants. Moreover, it is undisputed that MSN uses GRASTAR in a concentration and at a point in its tablet manufacturing process that is typical for a glidant.

MSN, however, argues that GRASTAR is not a glidant, but a diluent that was added to improve the disintegration and dissolution of its ANDA Products. But this assertion contradicts what MSN told the FDA about the effect of GRASTAR on flow characteristics and is not supported by the evidence. As Exelixis' formulation expert explained, GRASTAR is used in such a small concentration in MSN's ANDA Products that it would not have a meaningful impact as a diluent. Moreover, MSN's ANDA submission included an experiment showing that nearly doubling the amount of GRASTAR in its formulation had no impact on dissolution. And in any event, even if GRASTAR were also a diluent, formulation experts for both parties agreed that excipients can perform multiple functions. So GRASTAR could be both a diluent and a glidant.

MSN's ANDA Products thus directly infringe claim 3 of the '349 patent. MSN will also induce infringement of claim 3 of the '349 patent by virtue of its contractual arrangement with Zydus Worldwide DMCC ("Zydus") (the entity that will import, offer for sale, and sell MSN's

ANDA Products in the United States) and its proposed label relating to the use of MSN's ANDA Products.

IV. CLAIM 3 OF THE '349 PATENT

Claim 3 of the '349 patent claims a tablet pharmaceutical composition that includes cabozantinib (L)-malate, a filler, disintegrant, lubricant, and glidant, and is free of the 1-1 impurity. FOF ¶ 13.

V. ARGUMENT

A. Legal Standards for Infringement

Under the Hatch-Waxman Act, "if a product that an ANDA applicant is asking the FDA to approve for sale falls within the scope of an issued patent, a judgment of infringement must necessarily ensue." *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1278 (Fed. Cir. 2013); *see* 35 U.S.C. § 271(e)(2)(A). "A patent is directly infringed when a person 'without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent.'" *United Therapeutics Corp. v. Liquidia Techs., Inc.*, 74 F.4th 1360, 1367 (Fed. Cir. 2023) (quoting 35 U.S.C. § 271(a)). Further, whoever actively induces infringement of a patent shall be liable as an infringer. 35 U.S.C. § 271(b). Inducement requires a showing that the alleged infringer knew of the patent, knowingly induced the infringing acts, and possessed a specific intent to encourage another's infringement of the patent. *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1328 (Fed. Cir. 2009).

Determination of direct or induced infringement "is based on consideration of all the relevant evidence, including the ANDA filing, other materials submitted by the accused infringer to the FDA, and other evidence provided by the parties." *Abbott Labs. v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002). A patentee may prove infringement by "any method of analysis

that is probative of the fact of infringement." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1372 (Fed. Cir. 2009) (quoting *Forest Labs. v. Abbott Labs.*, 239 F.3d 1305, 1312 (Fed. Cir. 2001)); *see also Bristol-Myers Squibb Co. v. Aurobindo Pharma USA Inc.*, 477 F. Supp. 3d 306, 346-47 (D. Del. 2020) (finding that, while the plaintiffs' expert did not perform particle size measurements on the defendant's ANDA product, the expert's conclusion that the product satisfied the claimed particle size limitation was sufficiently supported by analysis of the manufacturing process and well-known principles of crystallization), *aff'd sub nom. Bristol-Myers Squibb Co. v. Sigmapharm Lab'ys, LLC*, 858 F. App'x 359 (Fed. Cir. 2021).

Given the statutory and regulatory requirements and consequences for submitting false statements in an ANDA, courts should assume that a filer has made accurate representations in its ANDA filings. *Vanda Pharms., Inc. v. Teva Pharms. USA, Inc.*, C.A. No. 18-651-CFC, 2022 WL 17593282, at *24 (D. Del. Dec. 13, 2022), *aff'd*, No. 2023-1247, 2023 WL 3335538 (Fed. Cir. May 10, 2023). "This principle that an ANDA filer is bound by the representations and specifications in its ANDA is central to the infringement inquiry." *Id*.

B. MSN's ANDA Products Infringe Claim 3 of the '349 Patent

MSN has stipulated that its ANDA Products are tablet pharmaceutical compositions (UF ¶ 65) that incorporate cabozantinib (L)-malate (UF ¶ 66), one or more fillers (UF ¶ 67), one or more disintegrants (UF ¶ 68), and one or more lubricants (UF ¶ 69). They are also essentially free of the 1-1 impurity. UF ¶ 70. As set forth below, Exelixis also established the last (and only contested) requirement—that MSN's ANDA Products include a "glidant."

1. Glidants Improve the Flow of a Drug Powder Mixture

The parties agree that the term "glidant" refers to a material that improves the flow of a drug powder mixture. Specifically,

- Exelixis' formulation expert, Dr. John Koleng, testified that a glidant is "a material added to a powder blend to improve the flow characteristics of the material." FOF ¶ 19 (Tr. 82:9-11 (Koleng)).

- MSN's formulation expert, Dr. Maureen Donovan, testified that "a glidant is a substance which improves the flow characteristics of a powder mixture." FOF ¶ 19 (Tr. 230:16-19 (Donovan)).

- MSN's Head of Formulations R&D, Mr. Ravikumar Nithiyanandam, testified, "A glidant is a chemical that improves the flow properties of a… blend." FOF ¶ 19 (Tr. 60:2-4 (Nithiyanandam)).

The definitions offered by the experts and Mr. Nithiyanandam are consistent with the two authorities on "pharmaceutical composition" cited in the '349 patent specification, "Remington: The Science and Practice of Pharmacy" and Swarbrick's "Encyclopedia of Pharmaceutical Technology." FOF ¶ 20.

Although Dr. Donovan also offered the opinion that glidants may work through one of several mechanisms set forth in the scientific literature (FOF ¶ 47), her definition of a glidant does not refer to any mechanisms at all. FOF ¶ 21. Nor do asserted claim 3, the '349 patent specification, or the references cited in the specification define a glidant with respect to any specific mechanism. FOF ¶ 21. In sum, there is no dispute that a glidant is a substance that improves the flow of the mixture to which it is added. FOF ¶ 19.

2. GRASTAR Improves the Flow Characteristics of MSN's ANDA Products

Statements and information in MSN's ANDA submission clearly demonstrate that GRASTAR improves the flow properties in its ANDA products and is thus a glidant.

a) The Cabozantinib API in MSN's ANDA Products Flows Poorly, a Circumstance in Which Glidants Are Commonly Used

As MSN explained in its Pharmaceutical Development Report ("PDR") submitted to the FDA, cabozantinib (L)-malate "exhibits poor flow properties." FOF ¶ 23. An API with poor flow

properties—where the powder does not mix evenly—can impact tablet uniformity. As Dr. Koleng explained, without adequate flow in the drug mixture, the amount of API may vary from tablet to tablet, resulting in inconsistent dosing, or tablets that dissolve in the body at different rates. FOF ¶ 24. As MSN's expert in clinical oncology, Dr. Anthony Mega, testified, achieving "consistency" is important. FOF ¶ 24.

Drs. Koleng and Donovan agreed that when the API is poorly flowing—as is the cabozantinib (L)-malate API here—glidants may be added to improve flow. FOF ¶ 25.

b) MSN Incorporates GRASTAR in its ANDA Products at a Stage in Manufacturing and in an Amount Typical of a Glidant

MSN's use of GRASTAR in manufacturing its ANDA Products is consistent with that of a glidant.

(i) GRASTAR is Added at the Pre-Lubrication Step

As described in its PDR, MSN's manufacturing begins with making granules in a process called "wet granulation." FOF ¶ 30. Powder materials including the API (cabozantinib), diluents (lactose monohydrate and corn starch), and a portion of the disintegrant (croscarmellose sodium) are delumped and sifted to ensure they are deagglomerated. FOF ¶ 30. The powders are then mixed with a binder solution (hydroxy propyl cellulose), dissolved in water, and dried to formed granules. FOF ¶ 30. Once the granules are formed, the extragranular excipients are added. FOF ¶ 31. During the pre-lubrication phase, the granules are mixed with granulated corn starch (GRASTAR) and a disintegrant (croscarmellose sodium). FOF ¶ 31. Next, a lubricant (magnesium stearate) is added, and the final mixture is compressed into tablets. FOF ¶ 31. GRASTAR is thus added during the pre-lubrication step, just prior to compression. FOF ¶ 34.

The step at which GRASTAR is added in MSN's manufacturing process supports the conclusion that it is a glidant. FOF ¶ 35. Dr. Koleng testified that glidants are typically added "in

the dry state just prior to compression (that is during the lubrication step)," (Tr. 83:23-84:3 (Koleng)), and cited scientific literature saying the same thing (including the Remington reference cited by the '349 patent). FOF ¶ 33. And even Dr. Donovan agreed that glidants are usually added after granulation, during the pre-lubrication stage of the tablet manufacturing process. FOF ¶ 33. MSN adds GRASTAR at precisely the same stage at which Exelixis adds a glidant in manufacturing Cabometyx®. FOF ¶ 34.

(ii) The Concentration of GRASTAR in MSN's ANDA Products is Typical of a Starch Glidant

As set forth in MSN's ANDA and confirmed by both formulation experts, MSN adds GRASTAR at a concentration of 9.71% of the total drug mixture. FOF ¶ 28. According to the scientific literature, starch and starch derivatives (like GRASTAR) are known glidants, and 9.71% is within the range typical for starch glidants. FOF ¶¶ 26, 28. The Swarbrick reference cited in the '349 patent and other references, including the Lachman textbook on pharmaceutical formulation, describe starch and starch derivatives being used as glidants at a range of 10% or less. FOF ¶ 28. As Dr. Koleng explained, the 9.71% concentration of GRASTAR in MSN's ANDA Products further supported his opinion that "granulated corn starch is a glidant in this formulation." FOF ¶ 29 (Tr. 106:6-13 (Koleng)).

c) MSN Told the FDA that Granulated Corn Starch Plays an Important Role in the Flow Characteristics of its Formulation

MSN submitted an ANDA that provided a detailed description of its proposed ANDA Products. UF ¶¶ 63-64; FOF ¶ 22. In its ANDA, MSN repeatedly told the FDA that GRASTAR improves the flow of its formulation. MSN's statements to FDA, which the company's Head of Formulation Research and Development admitted were truthful (FOF ¶ 22), provide compelling evidence that GRASTAR is a glidant. FOF ¶¶ 37, 40, 42.

In the Initial Risk Assessment portion of its PDR, MSN submitted a table describing the materials used in its ANDA formulation. FOF ¶ 36. As Dr. Koleng explained, this type of table is generated once a core formulation has been identified. FOF ¶ 36. In the section of the table concerning GRASTAR, MSN expressly stated that "***Granulated Corn Starch*** is used as a diluent in minimal concentration and ***it enhances the flowability of the granules***." FOF ¶ 36 (DTX-215 at 36 (emphasis added)). Although both Mr. Nithiyanandam and Dr. Donovan attempted to minimize this statement as simply describing the scientific literature, (Tr. 61:17-62:9 (Nithiyanandam); Tr. 227:14-228:3 (Donovan)), there is no reference to literature in the statement, which is written in the present tense. FOF ¶ 36.

In the Formula Optimization section of its PDR, MSN described a study regarding optimization of the level of GRASTAR in its ANDA Products. FOF ¶ 38. Specifically, MSN studied formulations of generic cabozantinib (L)-malate with concentrations of GRASTAR ranging from 6.7% to 12.7%. FOF ¶ 38. MSN began the section by stating that "***[t]he level of Granulated corn Starch plays an important role in flow characteristics***." FOF ¶ 39 (DTX-215 at 58 (emphasis added)). MSN's Mr. Nithiyanandam confirmed that this statement was based on studies done by MSN. FOF ¶ 39. MSN's statements to FDA were thus not merely characterizing the literature. FOF ¶ 39.

MSN's Justification for Microbial Method Validation—which assessed the quality of various grades of corn starch, including granulated corn starch (GRASTAR)—also stated: "***[s]tarch are [sic] used*** in pharmaceutical industry for a wide variety of reasons, such ***as an excipient in tablet and capsule [sic] as a diluent, as a glidant or as binder***." FOF ¶ 41 (PTX-724 at 1-2 (emphasis added)). And while MSN attempts to dismiss this statement as not relevant to GRASTAR, the prior page of the document expressly references GRASTAR. FOF ¶ 41.

MSN has not withdrawn, corrected, or amended any of the statements it made to the FDA about GRASTAR. FOF ¶ 36. And in fact, MSN's representations that GRASTAR improved flow are consistent with what a person of ordinary skill in the art would expect, and consistent with observations by GRASTAR's manufacturer, which performed testing showing that use of GRASTAR resulted in improved flowability of a poorly flowing API. FOF ¶¶ 43, 51. As even Dr. Donovan conceded, GRASTAR "would be expected that the addition of GRASTAR could improve the flow properties if that actually had been the case." FOF ¶ 27 (Tr. 217:21-24 (Donovan)). Thus, "it would be expected, even before experiments, to potentially enhance the flowability of the granules." FOF ¶ 27 (Tr. 237:7-9 (Donovan)). MSN's efforts to sidestep the representations in its ANDA are unavailing.

During closing argument, MSN also argued that data in an MSN laboratory notebook comparing two formulation prototypes supposedly showed that flow worsened when unmodified corn starch was replaced with GRASTAR in the extragranular layer. Tr. 1043:23-1047:17. But MSN's reliance on the data in the laboratory notebook is misplaced. First, as Dr. Koleng explained, the prototype study on which MSN relies has an error of unidentified origin and is thus unreliable.[1] FOF ¶¶ 55-58. Second, the data indisputably pertain to prototype formulations, not MSN's final ANDA Products. FOF ¶¶ 55-56; *see Reckitt Benckiser Pharm., Inc. v. Watson Labs.*, C.A. Nos. 13-1674-RGA, 14-422-RGA, 2016 WL 3186659, at *13 (discounting data from prototype formulations proffered as evidence of the final ANDA product's infringement), *aff'd on*

[1] The notebook includes numerical values for bulk density, tap density, Carr Index and Hausner ratio for two prototype formulations. FOF ¶¶ 55, 56. Bulk and tap density data are used to calculate Carr Index and Hausner ratios, common measurements of flow characteristics. FOF ¶ 56. However, there is a discrepancy between the figures in the MSN notebook. FOF ¶ 57. As Dr. Koleng explained, he could not identify the source of the discrepancy and thus determined that he could not rely on the flow data in the notebook. FOF ¶¶ 56, 58. Dr. Donovan did not address the discrepancy in her testimony about the data from the laboratory notebook. FOF ¶ 58.

other grounds sub nom. Indivior Inc. v. Dr. Reddy's Labs., S.A., 930 F.3d 1325 (Fed. Cir. 2019). Third, as the Court observed during closing arguments, such data, even if credited, would simply show that GRASTAR, a corn starch derivative, is not as effective a glidant as unmodified corn starch, another well-documented glidant. FOF ¶¶ 26, 59. That does not prove that GRASTAR is not a glidant.

MSN also attempts to distance itself from the statements made in its ANDA submission by arguing that the statements were not about its actual ANDA Products, but simply summarizing scientific literature about starch. Tr. 61:17-62:2 (Nithiyanandam). Importantly, this argument simply cannot be reconciled with the plain language of MSN's PDR, which even MSN's own expert admitted "summarizes the development of ***MSN's ANDA products***." FOF ¶ 22 (Tr. 235:9-11 (Donovan) (emphasis added)). Moreover, even if some of the statements are, as MSN suggests, characterizing the literature, there can be no doubt that MSN repeatedly told the FDA that GRASTAR was a known glidant. As Dr. Koleng explained, the Lachman textbook on pharmaceutical formulation—on which both parties rely—identifies "starch" (generally) and "Starch 1500" (which is a pregelatinized corn starch like GRASTAR) as "commonly used glidants." FOF ¶¶ 26, 27.

MSN's statements to FDA prove that the GRASTAR in MSN's ANDA Products is a glidant. As the Federal Circuit reasoned in *Intendis GmbH v. Glenmark Pharm., Inc.*, 822 F.3d 1355 (Fed. Cir. 2016), the defendant's "repeated statements to the FDA that the claimed excipients function as penetration enhancers tend to show that one of skill in the art would understand the claimed excipients to function as penetration enhancers" and found "***no reason why a district court acting as a fact finder should ignore a party's representation to a federal regulatory body that is directly on point.***" *Intendis*, 822 F.3d at 1362 (emphasis added); *see also Par Pharmaceuticals,*

Inc. v. Hospira, Inc., 835 F. App'x 578, 586 (Fed. Cir. 2020) (relying on statements in defendant's ANDA as evidence of infringement). Similarly, in *Vifor Fresenius Med. Care Renal Pharma Ltd. v. Teva Pharms. USA, Inc.*, 623 F. Supp. 3d 389 (D. Del. 2022), this Court found that "holding [defendant] to the representations made in its package insert and pharmaceutical development documents is appropriate." *Vifor Fresenius*, 623 F. Supp. 3d at 416, *appeal dismissed sub nom. Vifor Fresenius Med. Care Renal Pharma Ltd. v. Lupin Atlantis Holdings SA*, No. 2022-2253, 2023 WL 1794164 (Fed. Cir. Feb. 7, 2023); *see also Reckitt*, 2016 WL 3186659, at *20 (relying on statements in a defendant's ANDA to find a viscosity claim limitation infringed, even though the plaintiff did not offer its own evidence of viscosity with respect to that defendant, because the defendant's statements to the FDA satisfied the plaintiff's burden of proving infringement).

The instant case is similar to *Intendis* and *Vifor Fresenius*. MSN admits glidants that are used to improve the flow of a drug mixture and that cabozantinib was a poorly flowing API. It also admits that it told the FDA that GRASTAR played an important role in the flow characteristics of its drug mixture. FOF ¶¶ 36, 39. As in *Intendis*, there is no reason to ignore MSN's statements to FDA. *See Intendis*, 822 F.3d at 1362.

3. MSN's Additional Arguments Are Wrong on the Facts and the Law

MSN's expert Dr. Donovan maintains that even if the GRASTAR in MSN's formulation has a meaningfully positive impact on the flow of the MSN powder blend, it is not necessarily a glidant. Tr. 217:10-18 (Donovan). She offered four arguments to support this assertion, none of which is sufficient to overcome the evidence of infringement.

First, Dr. Donovan contends that the GRASTAR in MSN's ANDA Products is being used as a diluent, not a glidant. Tr. 186:21-187:10, 236:17-237:9 (Donovan). But the fact that MSN refers to GRASTAR as a diluent in its ANDA does not disqualify it as a glidant. Importantly, as Dr. Koleng explained, the "minimal concentration" at which GRASTAR is added to MSN's drug

mixture suggests it would not have a substantial impact as a diluent if that were its sole function. FOF ¶ 44. Moreover, as both experts agreed, excipients can be multi-functional. FOF ¶ 45. There is thus no reason to conclude that an excipient that improves flow but is called a diluent is also not a glidant.

Second, MSN argues that its wet granulation process rendered a glidant unnecessary. Tr. 209:8-20 (Donovan). But Dr. Donovan admitted that glidants can be used to improve flow even after wet granulation. FOF ¶ 32. And Dr. Koleng testified that he has ***often*** used a glidant in such circumstances, especially where (as here) the granules are fine. FOF ¶ 32. Indeed, Exelixis adds its glidant after wet granulation in manufacturing Cabometyx®. FOF ¶ 33.

Third, according to MSN, GRASTAR was added to its formulation to improve dissolution. Tr. 63:20-64:5, 64:16-19 (Nithiyanandam); Tr. 215:20-216:24 (Donovan). But this is belied by MSN's own data. The PDR study on which Dr. Donovan relies compared dissolution rates of formulations with varying levels of GRASTAR in the drug mixture: "low" (6.7%), "optimum" (9.7%), and "high" (12.70%) concentrations. FOF ¶ 46. This study concluded that: "Based on the above results, ***no significant difference was observed in the dissolution profiles*** of cabozantinib tablets" with varying levels of GRASTAR. FOF ¶ 46 (DTX-215 at 60 (emphasis added)). These results do not support the argument that GRASTAR had an effect on the dissolution of the mixture. FOF ¶ 46.

Finally, MSN's expert testified that to prove an excipient is a glidant, there must be evidence that the excipient is improving flow through one of five purported mechanisms: (1) reducing electrostatic forces; (2) adsorbing fine particles; (3) absorbing environmental gases; (4) reducing van der Waals interactions; and (5) coating / adherence. FOF ¶ 47. MSN has no support for this "mechanism" theory, which it failed to advance during claim construction. There is no

glidant mechanism required by the patent, the specification, or the scientific literature. FOF ¶ 21. In fact, MSN's additional "proof" requirement is inconsistent with its own proffered definition of a "glidant," which does not require a glidant to operate by any specific mechanism. FOF ¶ 21. As Dr. Koleng explained, glidants are not defined by any specific mechanism. FOF ¶¶ 19, 21.

Even if the Court were to accept this added requirement, Dr. Koleng testified the GRASTAR in MSN's ANDA Products more likely than not improves flow through at least one of the mechanisms identified by Dr. Donovan, including by adsorbing fine particles in the drug mixture. FOF ¶¶ 48-54.

In sum, MSN's various arguments in this litigation stand in sharp contrast with its clear and admittedly true representations to the FDA that GRASTAR plays an important role in the flow characteristics of its ANDA Products. MSN's representations to the FDA are directly on point and prove infringement. *See Intendis*, 822 F.3d at 1362.

C. MSN Will Also Induce Infringement of Claim 3 of the '349 Patent

In addition to directly infringing claim 3 of the '349 patent, MSN will induce infringement by manufacturing and supplying its ANDA Products to Zydus for distribution to doctors and patients in the United States. *See Vita-Mix Corp.*, 581 F.3d at 1328; 35 U.S.C. § 271(b).

First, there is no dispute that MSN was and is aware of the '349 patent. FOF ¶¶ 6, 61. Second, there is no dispute that MSN has entered into a license and supply agreement with Zydus, whereby MSN has agreed to supply Zydus with MSN's ANDA Products for importation and sale in the United States. UF ¶ 71; FOF ¶ 60. And third, MSN plainly possesses the requisite intent for induced infringement. MSN was and is aware of Exelixis' particularized infringement allegations, which are based on MSN's own admissions to the FDA in its ANDA on the use of GRASTAR as a glidant. FOF ¶ 61; *see supra* at pp. 8-12. Nonetheless, MSN's label encourages doctors to prescribe and patients to use MSN's ANDA Products in the United States. FOF ¶ 60.

By supplying MSN's ANDA Products to Zydus for importation into, use, offer for sale, and/or sale in the United States, prior to the expiration of the '349 patent, MSN will induce the direct infringement of claim 3 of the '349 patent, including by Zydus, healthcare professionals, and/or patients in the United States.

VI. CONCLUSION AND REMEDIES

For the reasons above, Exelixis respectfully requests that the Court find that making, using, offering to sell, selling, or importing MSN's ANDA Products into the United States, will literally infringe claim 3 of the '349 patent and, therefore, that the submission of MSN's ANDA seeking approval to market MSN's ANDA Products before expiration of the '349 patent infringes that claim under 35 U.S.C. § 271(e)(2)(A); and that, upon FDA approval, MSN will directly infringe that claim under 35 U.S.C. § 271(a), and will induce infringement of that claim under 35 U.S.C. § 271(b). Exelixis further requests that the Court enter an order pursuant to 35 U.S.C. § 271(e)(4)(A) providing that the effective date of any approval of MSN's ANDA shall be a date which is not earlier than the latest expiration date of the Patents-in-Suit, including any extensions and/or additional periods of exclusivity to which Exelixis is or becomes entitled, and an order permanently enjoining MSN, its affiliates, subsidiaries, and each of its officers, agents, servants and employees and those acting in privity or concert with them, from making, using, offering to sell, selling, or importing into the United States MSN's ANDA Products, or inducing such activity by others including but not limited to Zydus, until after the latest expiration date of the Patents-in-Suit, including any extensions and/or additional periods of exclusivity to which Exelixis is or becomes entitled.

OF COUNSEL:

William F. Lee
Lisa J. Pirozzolo
Emily R. Whelan
Kevin S. Prussia
Marissa A. Lalli
Kevin M. Yurkerwich
Jonathan A. Cox
Amy L. Mahan
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

Amy K. Wigmore
Gerard A. Salvatore
WILMER CUTLER PICKERING
HALE AND DORR LLP
1875 Pennsylvania Avenue, NW
Washington, DC 20006
(202) 663-6000

Charlotte Geaghan-Breiner
WILMER CUTLER PICKERING
HALE AND DORR LLP
2600 El Camino Real, Suite 400
Palo Alto, CA 94306
(650) 858-6000

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MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/Jack B. Blumenfeld

Jack B. Blumenfeld (#1014)
Anthony D. Raucci (#5948)
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899
(302) 658-9200
jblumenfeld@morrisnichols.com
araucci@morrisnichols.com

Attorneys for Plaintiff Exelixis, Inc.

CERTIFICATE OF SERVICE

I hereby certify that on December 12, 2023, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on December 12, 2023, upon the following in the manner indicated:

Dominick T. Gattuso, Esquire — *VIA ELECTRONIC MAIL*
HEYMAN ENERIO GATTUSO & HIRZEL LLP
300 Delaware Avenue, Suite 200
Wilmington, DE 19801
Attorneys for Defendants MSN Laboratories Private Limited and MSN Pharmaceuticals, Inc.

George C. Lombardi, Esquire — *VIA ELECTRONIC MAIL*
Bryce A. Cooper, Esquire
Kurt A. Mathas, Esquire
Kevin J. Boyle, Esquire
Brian O'Gara, Esquire
Elizabeth E. Grden, Esquire
WINSTON & STRAWN LLP
35 West Wacker Drive,
Chicago, IL 60601-9703
Attorneys for Defendants MSN Laboratories Private Limited and MSN Pharmaceuticals, Inc.

/s/ Jack B. Blumenfeld

Jack B. Blumenfeld (#1014)